

Claims

1. A method for determining whether a treatment of a disorder with an HDAC inhibitor is to be started/continued or not comprising
 - (a) contacting a sample derived from tissue affected by the disorder with an antibody capable of binding to acetylated histone but not to deacetylated histone;
 - (b) determining the level of histone acetylation in the sample; and
 - (c) classifying the disorder as to be treated with an HDAC inhibitor when the level of histone acetylation is significantly lower than that of a reference sample.
2. A method according to claim 1 wherein the antibody is capable of binding to acetylated human histone H4 but not to deacetylated human histone H4, and the level of human histone H4 acetylation is determined in step (b).
3. A method according to claim 1 or 2 wherein the antibody is a monoclonal antibody.
4. A method according to claim 3 wherein the antibody is the antibody T25 which is obtainable from the cell line G2M-T25-H4ac deposited at DSMZ.
5. A method according to claim 3 wherein the antibody is the antibody T52 which is obtainable from the cell line G2M-T52-ac deposited at DSMZ.
6. A method according to anyone of claims 1 to 5 wherein the disorder is selected from the group consisting of diseases in which the induction of hyperacetylation of histones has a beneficial effect resulting in differentiation and/or apoptosis of a patient's tumor cells, diseases that show aberrant recruitment of HDAC activity, conditions associated with abnormal gene expression, autoimmune diseases, and proliferative diseases.
7. A method according to claim 6 wherein the disorder is selected from the group consisting of skin cancer, melanoma, estrogen receptor-dependent and independent breast cancer, ovarian cancer, testosterone receptor-dependent and independent prostate cancer, renal cancer, colon and colorectal cancer, pancreatic cancer, bladder cancer, esophageal cancer, stomach cancer, genitourinary cancer, gastrointestinal cancer, uterine cancer, astrocytomas, gliomas, basal cancer and squameous cell carcinoma, sarcomas as Kaposi's sarcoma and osteosarcoma, head and neck cancer,

small cell and non-small cell lung carcinoma, leukemia, lymphomas and other blood cell cancers, and thyroid resistance syndrome.

8. A method according to anyone of claims 1 to 7 wherein in step (b) the level of histone acetylation in the sample is determined by flow cytometry, immunohistochemistry, ELISA and/or Western Blotting.
9. A method according to anyone of claims 1 to 8 wherein the reference sample is a sample derived from tissue from a healthy individual said tissue from a healthy individual corresponding to the tissue affected by the disorder wherein the reference sample is processed according to steps (a) and (b).
10. A method according to anyone of claims 1 to 8 wherein the reference sample is a further sample derived from tissue affected by the disorder which has been contacted with an HDAC inhibitor wherein the reference sample is processed according to steps (a) and (b).
11. The use of an antibody capable of binding to acetylated histone for
 - determining whether a treatment of a disorder with an HDAC inhibitor is to be started/continued or not; and/or
 - the classification of tumors.
12. An antibody capable of binding to peptides having the sequence as shown in SEQ ID NO:4 and SEQ ID NO:5 but not to anyone of the peptides having the sequences as shown in SEQ ID NO:6, SEQ ID NO:2, SEQ ID NO:10 and SEQ ID NO:11.
13. An antibody capable of binding to peptides having the sequence as shown in SEQ ID NO:4 and SEQ ID NO:5 and SEQ ID NO:6 but not to peptides having the sequence as shown in SEQ ID NO:2.
14. An antibody produced by a hybridoma cell line selected from hybridoma cell lines G2M-T25-H4ac and G2M-T52-ac deposited at DSMZ.
15. A hybridoma cell line producing an antibody according to claim 12 or 13.

16. A hybridoma cell line which has the identifying characteristics of the cell line G2M-T25-H4ac deposited at DSMZ.
17. A hybridoma cell line which has the identifying characteristics of the cell line G2M-T52-ac deposited at DSMZ.
18. A diagnostic kit for determining the level of histone acetylation containing
 - (i) an antibody capable of binding to acetylated histone but not to deacetylated histone;
 - (ii) an HDAC inhibitor; and optionally
 - (iii) a secondary antibody directed against the antibody of step (i); and optionally
 - (iv) reagents for the measurement of a signal derived from an antibody binding to acetylated histones.
19. A diagnostic kit according to claim 19 wherein the antibody is the monoclonal antibody termed T25 or the monoclonal antibody termed T52.
20. The use of the antibodies T25 and/or T52 to direct substances conjugated to these antibodies to sites of histone hyperacetylation.
21. A use according to claim 20 wherein conjugated substances are radioactive compounds.
22. A use according to claim 20 wherein conjugated substances are chemotherapeutic or cytotoxic agents.
23. A use according to anyone of claims 20 to 22 wherein conjugated substances are released by proteolytic cleavage.